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REMARKS

Claims 1-61 remain in the application. Claims 1, 14, 37, 53 are in independent form.

Claims 3-9, 11, 12, 15-22, 33, and 34 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting, as being unpatentable over claims 7-10, 16-26, 57, and 58 of copending application Serial No. 10/122,611. A Terminal Disclaimer has been attached hereto, thereby rendering the present rejection moot. Reconsideration of the rejection is respectfully requested.

Claims 1-61 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicants regard as the invention. With regard to claims 1-61, the Office Action states that the claims as written are ambigious because the claims appear to be somewhat inconsistent with the specification.

The Office Action states that the claims as written require a metal, chelating group, and a gastrin releasing peptide (GRP) that includes a bombesin agonist-binding moiety. When read more specifically, the claims require a metal, chelating group, and a GRP, such that the GRP includes therein a bombesin agonist-binding moiety, thus the claims require four groups while the specification only lists three. There are only three components in the compound and not four because part of the GRP is the bombesin agonist-binding moiety. In other words, the GRP includes bombesin agonist-binding moiety within the peptide and the two parts are therefore not separate units, but rather a single unit. The compound is specifically disclosed in the specification on page 13, line 19, through page 14, line 6. As this compound structure is specifically disclosed throughout the specification, reconsideration of the rejection is respectfully requested.

Claims 4, 6, 11, 17, 19, 33, 41, 42, 49, 50, 58, 60, and 61 are rejected as being ambiguous because of the phrase "derivatives thereof." The Office Action states that the claims are ambiguous because one cannot readily ascertain which portions of the parent compound are retained in the derivatives. As disclosed in the specification on page 8, lines 10-33, the scope of the term "chelator" is delineated. Specifically, there are disclosed numerous chelators that can be utilized and also there is a list of references that disclose additional chelators that can be used. On page 10, line 29 of the specification, there is disclosed a metal complex and chelators, including chelator backbones, that complex the radionuclide metals. The listing also includes chelator backbones that complex the beta particle emitting radionuclide metals. There is therefore sufficient description in the specification regarding what is encompassed by the term "chelator" or the phrase "chelator derivatives." Since there is proper disclosure in the specification for the phrase "derivatives thereof," reconsideration of the rejection is respectfully requested.

Claims 1-7, 11, 12, 14-20, 33, 34, 37-43, 46-51, and 53-58stand rejected under 35 U.S.C. §103(a) as obvious over the Albert et al. patent in view of the Edwards et al. patent and further in view of the Srinivasan et al. patent.

It is Hornbook Law that before two or more references may be combined to negative patentability of a claimed invention, at least one of the references must teach or suggest the benefits to be obtained by the combination. This statement of law was first set forth in the landmark case of Ex parte McCullom, 204 O.G. 1346; 1914 C.D. 70. This decision was rendered by Assistant Commissioner Newton upon appeal from the Examiner-in-Chief and dealt with the matter of combination of references. Since then many courts have, over the years, affirmed this doctrine.

The applicable law was more recently restated by the Court of Appeals for the Federal Circuit in the case of ACS Hospital Systems, Inc. v. Montefiore Hospital, 732 F.2d 1572,1577, 221 U.S.P.Q. 929 (Fed. Cir. 1984). In this case the Court stated, on page 933, as follows:

> Obviousness cannot be established by combining the teachings of the prior art to produce the claimed invention, absent some teaching or suggestion supporting the combination. Under Section 103 teachings of references can be combined only if there is some suggestion or incentive to do so. The prior art of record fails to provide any such suggestion or incentive. Accordingly we hold that the court below erred as a matter of law in concluding that the that the claimed invention would have been obvious to one of ordinary skill in the art under section 103.

This Doctrine was even more recently reaffirmed by the CAFC in Ashland Oil, Inc. v. Delta Resins and Refractories, Inc., et al., 776 F.2d 281,297, 227 U.S.P.Q. 657,667. As stated, the District Court concluded:

> Obviousness, however, cannot be established by combining the teachings of the prior art to produce the claimed invention unless there was some teaching, suggestion, or incentive in this prior art which would have made such a combination appropriate.

The Court cited ACS Hospital Systems, Inc. in support of its ruling. This Doctrine was reaffirmed in In re Deuel, 34 USPQ2d 1210 (Fed. Cir. 1995).

The Office Action states that the Albert et al. patent discloses biologically active peptides selected from growth factors, peptide hormones, interferon, and cytokines that bear at least one chelating group linked to an amino group of the peptide. In addition, the chelating group is capable of complexing with a detectable

element for use as a pharmaceutical (radiopharmaceutical for *in vivo* imaging or targeting tissues or therapy). However, when read more specifically, the Albert et al. patent does not disclose the use of an agonist. Additionally, the Office Action states that it would have been obvious to one of ordinary skill in the art, at the time the invention was made, to use the gastrin releasing hormone because in claim 1 of the Albert et al. patent, the biologically active peptides may be selected from growth factors, insulin, LHRH, GRP etc. The Office Action concludes that a skilled practitioner in the art would be motivated to select one of the peptides listed by the Albert et al. patent to be conjugated to a chelating group in a detectable label. However, as stated previously, GRP is considered to be an autocrine growth factor as established by the attached Walsh et al., 1991, article. GRP has been shown to stimulate the growth of cells in culture and tumors and is therefore considered to be an agonist. Many individuals skilled in the art have been hesitant to use this compound in treating cancer based on the propensity of the GRP to stimulate growth. The growth stimulation occurs because the binding of GRP receptor agonists increases the rate of cell division. A great deal of work has been and is being pursued to develop BBN or GRP analogs that are antagonists, as stated in the present application at page 3, line 14, through page 4, line 1. The bombesin analogs that are used in the Alfred et al. patent are therefore antagonists, not agonists. Antagonists are created by removing the final amino acid and amidating the compound, thereby producing antagonists that can be used *in vivo* to block agonists. Accordingly, a skilled practitioner in the art would not be motivated to select the agonist form of bombesin for use in treating patients.

Further, the Albert et al. patent discloses a biologically active peptide comprising at least one chelating group capable of being complexed with a radiolabled. While the reference discloses that the biologically active peptide may be bombesin and bombesin antagonists or gastrin, the reference does suggest or disclose a GRP agonist having a bombesin agonist moiety that is administered in the treatment or imaging of neoplastic diseases (i.e., tumors). Also, the Albert et al. patent fails to disclose the combination GRP agonist having bombesin agonist

moiety as claimed by Applicants. Instead, biogically active peptide disclosed in the Albert et al. patent may be either bombesin and bombesin antagonist or GRP, not a combination of the two.

The Edwards et al. patent pertains to non-radioactive treatments for use in cancer therapy, as stated at column 16, lines 10-20. The Edwards et al. patent deals with normal tissue growth, not the growth suppression of malignant, cancerous or otherwise harmful tissues. The Edwards et al. patent discloses that agonists are used for tissue growth (see column 15, line 17) because agonists elicit mitogenic responses in the tissues to which the agonists are administered. Further, the Edwards et al. patent discloses an iodinated phenyl releasing peptide in combination with the bombesin receptor, and such a combination does not include a chelator. Given this explicit teaching, there is no teaching or suggestion for the use of an agonist in a radiopharmaceutical treatment as recited in the presently pending independent claims.

The Office Action further states that the Srinivasan et al. patent discloses metal radionuclide chelating compounds. More specifically, the Srinivasan et al. patent discloses that targeting agents such as bombesin may be conjugated to various chelators. However, there is no disclosure that the compound is a bombesin agonist. It was known to those of skill in the art to use a bombesin antagonist as disclosed above. However, individuals skilled in the art specifically avoided using a bombesin agonist because the agonist was thought to be detrimental when administered *in vivo*. Therefore, the compound referred to in the Srinivasan et al. patent was a bombesin antagonist and not a bombesin agonist.

Since none of the patents alone or in combination discloses or suggests the compound of the presently pending claims, the presently pending claims are patentable over the cited prior art references and reconsideration of the rejection is respectfully requested.

The remaining dependent claims not specifically discussed herein are ultimately dependent upon the independent claims. References as applied against these dependent claims do not make up for the deficiencies of those references as discussed above. The prior art references do not disclose the characterizing features of the independent claims discussed above. Hence, it is respectfully submitted that all of the pending claims are patentable over the prior art.

In view of the present amendment and foregoing remarks, reconsideration of the rejections and advancement of the case to issue are respectfully requested.

The Commissioner is authorized to charge any fee or credit any overpayment in connection with this communication to our Deposit Account No. 11-1449.

Respectfully submitted,

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I hereby certify that this correspondence is being deposited with the United States Postal Service "Express Mail Post Office to Addressee" addressed to the Assistant Commissioner for Patents, Washington, D.C. 20231 on October 18, 2002.

Angel Webb

VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE CLAIMS:

1. A compound comprising a metal complexed with a chelating group attached to a gastrin releasing peptide (GRP) receptor agonist, [which] the gastrin releasing peptide receptor agonist includ[es]ing a bombesin agonist moiety.

14. A complex comprising a metal and a compound having a structure of the formula X-Y-B wherein X is a metal chelating group, Y is a spacer group or covalent bond and B is a gastrin releasing peptide receptor GRP agonist, [which] the GRP receptor agonist includ[es]ing a bombesin agonist moiety.

37. A method of treating patients using radioisotope therapy by administering an effective amount of a pharmaceutical comprising a metal complex with a chelating group with a GRP [gastrin releasing peptide] receptor agonist, [which] the GRP receptor agonist includ[es]ing a bombesin agonist moiety.

53. A method of forming a therapeutic or diagnostic compound comprising the step of reacting a metal complexed with a chelating group with a GRP receptor agonist [which] the GRP receptor agonist includ[es]ing a bombesin agonist moiety.